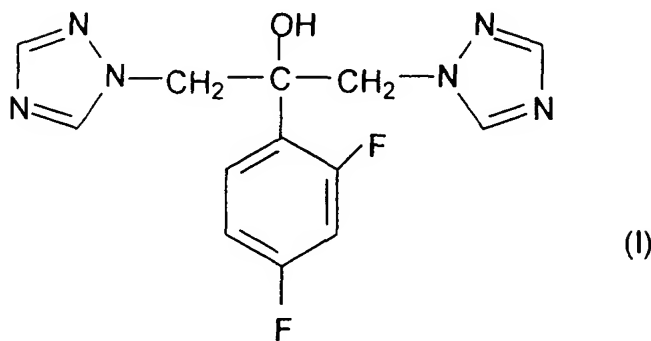


What we claim is

- 1 1. A process for the synthesis of monohydrate and crystal modifications
2 of fluconazole of formula (I)

3



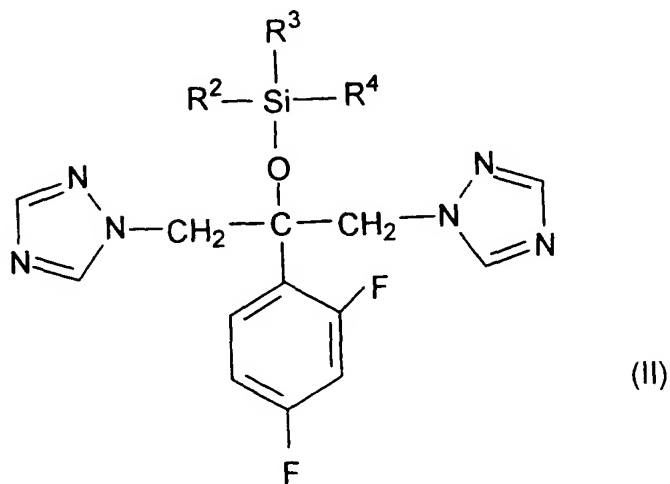
4

comprising the steps of:

5

- a.) hydrolyzing a silyl ether derivative of formula (II)

6



7 - wherein the meaning of R^2 is hydrogen, or a C_1-C_{10} alkyl or phenyl group,
8 R^3 and R^4 independently of each other are a C_1-C_{10} alkyl or phenyl group -
9 at a pH preferably either below 3 or above 8 in an aqueous solution,

10 then cooling the obtained reaction mixture containing the fluconazole
11 of formula (I) and isolating the precipitated fluconazole monohydrate and
12 optionally

13 dissolving the fluconazole monohydrate obtained from the hydrolysis of
14 silyl-fluconazole in a C_1-C_4 straight or branched chain alcohol at boiling
15 temperature and cooling the solution with a speed of 5-15 °C/h to obtain the
16 crystal modification II of fluconazole, or

17 b.) dissolving anhydrous fluconazole or monohydrate of it in a C_1-C_4
18 straight or branched chain alcohol at boiling temperature and cooling the
19 solution with a speed of 5-15 °C/h to obtain the crystal modification II of
20 fluconazole, or

21 c.) drying slowly fluconazole monohydrate after seeding preferably with
22 seeding crystals of crystal modification II at 30-70 °C, preferably in vacuum
23 to obtain the crystal modification II of fluconazole, or

24 d.) drying fast fluconazole monohydrate after seeding preferably with
25 seeding crystals of crystal modification I at 80 °C, to obtain the crystal
26 modification I of fluconazole.

1 2. The process according to claim 1, characterized by carrying out the
2 hydrolysis of silyl ether derivatives of formula (II) - wherein the
3 meaning of R^2 , R^3 and R^4 is as defined in claim 1 - in aqueous methanolic
4 solution in the presence of sodium hydroxide.

1 3. The process according to claim 1, characterized by carrying out the
2 hydrolysis of silyl ether derivatives of formula (II) - wherein the
3 meaning of R^2 , R^3 and R^4 is as defined in claim 1 - in aqueous sodium
4 hydroxide solution.

1 4. The process according to claim 1, characterized by
2 using a silyl ether derivative of formula (II), wherein R^2 , R^3 and R^4 are
3 methyl groups, as starting material.

1 5. The process according to claim 1 for the synthesis of crystal
2 modification II of fluconazole, c h a r a c t e r i z e d b y cooling
3 the solution of anhydrous fluconazole or monohydrate of it in isopropanol
4 obtained at boiling temperature with a speed of 10 °C/h.

1 6. The process according to claim 1 for the synthesis of crystal
2 modification II of fluconazole, c h a r a c t e r i z e d b y cooling
3 the solution of anhydrous fluconazole or monohydrate of it in ethanol
4 obtained at boiling temperature with a speed of 10 °C/h.

1 7. The process according to claim 1 for the synthesis of crystal
2 modification II of fluconazole, c h a r a c t e r i z e d b y cooling
3 the solution of anhydrous fluconazole or monohydrate of it in sec-butanol
4 obtained at boiling temperature with a speed of 10 °C/h.

1 8. The process according to claim 5 c h a r a c t e r i z e d b y
2 cooling the solutions to 0 °C.

1 9. The process according to claim 1 for the synthesis of crystal
2 modification II of fluconazole, c h a r a c t e r i z e d b y drying
3 the fluconazole monohydrate in the presence of seeding crystals of crystal
4 modification II with stirring, in vacuum at 40 °C for 2 h, then at 70 °C
5 for 4 h.

1 10. The process according to claim 1 for the synthesis of crystal
2 modification I of fluconazole, c h a r a c t e r i z e d b y drying
3 the fluconazole monohydrate in the presence of seeding crystals of crystal
4 modification I with stirring, in vacuum at 80 °C for 4 h until the weight
5 is constant.